~~hybridisation and/or a wash carried out in 0.1xSSC-0.2xSSC buffer, 0.1% (w/v) SDS at a temperature of at least 55°C.~~ is substantially identical to the nucleotide sequence set forth in SEQ ID NO:9 or a sequence complementary to said sequence.

REMARKS

With the entry of the present Amendment, claims 79-85 and 88-95 are in this application. Claims 86-87 have been canceled without prejudice, and claims 85 and 95 have been amended to better claim the invention. The recitation of substantially identical is supported at page 23, lines 19-22 (of the substitute specification). None of the amendments made herein constitutes the addition of new matter.

The Rejections under 35 U.S.C. 112, first paragraph

Claims 79-95 have been rejected under 35 U.S.C. 112, first paragraph, as allegedly not enabled for coding sequences of 60, 80 or 90% nucleotide sequence identity to SEQ ID NO:10 or for a nucleic acid sequence which hybridizes to the nucleotide sequence of SEQ ID NO:9. Applicants respectfully traverse this rejection.

As a first matter, Applicants respectfully point out that claims 79-84 and 91-93 are limited with respect to the sequences associated with the claimed nucleic acid molecule. Applicants respectfully submit that these claims were mistakenly included with this rejection.

Applicants have presented a limited number of claims (85-90 and 95) reciting sequences having at least 60% or greater sequence identity to SEQ ID NO:10 and to specify that the encoded protein is an ecdysteroid receptor polypeptide which binds ecdysone when said receptor polypeptide is in contact with a USP polypeptide. This

limitation was discussed in the personal interview of June 27, 2002, and it was Applicants' understanding at that time that this level of sequence identity would be acceptable to the Patent Office.

The Examiner indicated in an informal telephone interview that examples of ecdysone receptors of at least 60% sequence identity to SEQ ID NO:10 would overcome the rejection. Applicants provide herewith the results of sequence comparisons in which two ecdysone receptor clones from *Nezara virdula* show 72.9 and 73.4% sequence identity to the exemplified SEQ ID NO:10 ecdysone receptor of *Myzus persicae*. See Exhibit A for a summary of these sequence comparisons. In addition, the ecdysone receptor from *Bemesia tabacai* shows 71.6% amino acid sequence identity to SEQ ID NO:10. See Exhibit B for the results of this sequence comparison. Accordingly, Applicants respectfully request withdrawal of the rejection. As argued previously, Applicants have provided adequate description – with respect to sequence relatedness and with the provision of an ecdysone binding assay readily carried out by one of ordinary skill in the art. Applicants maintain on the record that there would be no requirement for **undue** experimentation. One of ordinary skill in the art would be unlikely to construct random variants of the recited sequences and then test for binding activity, but rather one of ordinary skill in the art would be most likely to look to expressed sequences in an insect where ecdysone hormones are present. The required functional activity of an ecdysone receptor protein has been clearly set forth: ecdysone binding activity.

The Patent Office has further characterized the state of the art as being that "even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function, and that a single amino acid change in a protein's sequence can drastically affect the structure of a protein and the architecture of an entire cell," citing the example of sickle cell anemia.

In the interest of advancing prosecution and without acquiescing to the rejection, Applicants have amended claims 85 and 95 to recite sequences substantially identical to the specifically exemplified sequence. This is supported by page 23, lines 19-22 of the substitute specification. Although the Examiner makes statements relative to the potential importance of single amino acid changes, Applicants respectfully maintain that the art can readily make substitution mutations and test them, and only those sequences which encode a protein which binds ecdysteroid are within the scope of the claims.

In view of the high level of skill in the relevant art, the well known techniques for identifying sequences with the specified relatedness to the specific sequence, and the readily accessible methods for testing a protein for ligand binding (e.g., ecdysone binding), Applicants respectfully urge that the invention as claimed is adequately enabled by the as-filed Specification, taken with what is well known and readily accessible in the art.

Claims 79-95 have been rejected under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed, had possession of the invention. Applicants respectfully traverse this rejection.

As stated above, claims 79-84 and 91-94 recite specifically the exemplified sequences set forth in SEQ ID NOs:9 and 10 and/or SEQ ID NOs:11 and 12. With respect to the remaining claims, there are structural and functional limitations in the claims. With respect to claims 85-90 and 95, whether a particular sequence meets the structural limitation is readily determined by sequence comparison, using methodology well known to the art. These claims contain the functional limitation that the polypeptide must bind ecdysone, a representative insect ecdysteroid. Binding is also determined using techniques well known to the art. Proteins which do not, in the appropriate heterodimer, bind ecdysone are outside the metes and bounds of the claims. The application, at page

38, line 23, through page 39, line 2, provides guidance concerning conservative acid substitutions. This is well understood in the art, and variants produced can be tested using techniques well known to the art. Applicants respectfully maintain that the claims are adequately enabled when the Specification is taken together with the knowledge of the art.

Applicants respectfully maintain that the claims are adequately enabled when the Specification is taken together with the knowledge of the art.

In view of the amendments to the claims and the foregoing discussion, Applicants respectfully request the withdrawal of the rejections under 35 U.S.C. 112, first paragraph.

Conclusion

In view of the foregoing, it is submitted that this case is in condition for allowance, and passage to issuance is respectfully requested.

If there are any outstanding issues related to patentability, the courtesy of a telephone interview is requested, and the Examiner is invited to call to arrange a mutually convenient time.

This amendment is accompanied by a Petition for Extension of Time (two months) and a check in the amount of $450.00 as required by 37 C.F.R. 1.17. It is believed that this amendment does not necessitate the payment of any additional fees under 37 C.F.R. 1.16-1.17.

If the amount submitted is incorrect, however, please charge any deficiency or credit any overpayment to Deposit Account No. 07-1969.

Respectfully submitted,

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